REMARKS

In the foregoing claim amendments, claims 1-15, 21-23 and 27-36 have been amended. No new matter has been added. Now pending in the application are claims 1-50, of which claims 37-50 have been withdrawn from further consideration. Amongst claims 1-36, claims 1, 12, 22 and 28 are independent. The following comments address all stated grounds for rejection, and Applicants respectfully submit that the presently pending claims, as identified above, are now in a condition of allowance.

I.   Summary of Objections and Rejections

The specification is objected to because of minor informalities.

Claims 1-11 and 28-36 are rejected under 35 U.S.C. §101 as being drawn to non-statutory subject matter.

Claims 1-36 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite.

Claims 1-9, 11, 22-23, 25-27, 28-30 and 32-36 are rejected under 35 U.S.C. §102(b) as being anticipated by Goryanin *et al.* (Bioinfomatics, 1999, Vol. 15, No. 9, p.749-758).

Claims 1-2 and 10 are rejected under 35 U.S.C. §102(b) as being anticipated by DelaFuente *et al.* (Proceedings of the Second International Conference on System Biology, Pasadena, California, 2001, p213-221).

Claims 12-19 and 21 are rejected under 35 U.S.C. §102(e) as being anticipated by Potts *et al.* (U.S. Patent No. 6,882,940).

Claims 12-14 and 20-21 are rejected under 35 U.S.C. §103(a) as being unpatentable over DelaFuente *et al.* in view of Bubendorf *et al.* (Journal of Pathology, 2001, Vol. 195, p.72-79).

These objections and rejections will be discussed separately below.

II.   Claim Amendments

Claims 1 and 28 have been amended to recite a medium holding instructions executable in a computing device. Dependent claims 2-11 and 29-36 have also been amended to recite the medium of claims 1 and 28, respectively. Claim 12 has been amended to recite modifying the model of the biological process based on the data relating to the experiment. Claim 22 has been amended to recite computer-readable program means for gathering data relating to an in situ experiment of the biological process conducted on an experimental device. Support for the amendments is found in originally filed claims 1, 12, 22 and 28 and throughout the specification of the present application. No new matter has been added by the amendments.

III.   Specification

The specification has been objected to because it recited embedded hyperlinks and/or other form of browser-executable code (URLs). In response, Applicants have amended the specification to remove the URLs that were listed in the specification and to expand all related acronyms.

The Examiner requests that trademarks be capitalized and accompanied by the generic terminology in the specification. In response, Applicants have amended the specification to capitalize trademarks contained in the specification; all trademarks are believed to be accompanied by the generic terminology.

In view of the foregoing amendments to the specification, Applicants respectfully request that the Examiner withdraw the objections to the specification.

IV.   Claim Rejections under 35 U.S.C. §101

Claims 1-11 and 28-36 are rejected under 35 U.S.C. §101 as being drawn to non-statutory subject matter. Applicants respectfully traverse the rejection.

The Examiner notes (Office Action, page 4, lines 2-8) that:

> Claims 1-9 and 28-36 are directed to systems comprising a
> simulation engine and an analysis environment in communication

with said simulation engine. The system is not limited to comprise
any hardware element or <u>combination</u> of software and hardware
such that it is interpreted to be a physical article of manufacture.

In the forgoing amendments, Applicants have amended claims 1 and 28 to recite a
medium holding instructions executable in a computing device. In amended claims 1 and 28, the
medium includes instructions for a simulation engine and an analysis environment. Dependent
claims 2-11 and 29-36 have also been amended to recite the medium of claims 1 and 28,
respectively. As such, Applicants respectfully request that the Examiner withdraw the rejection
of claims 1-11 and 28-30 under 35 U.S.C. §101.

V.   Claim Rejections under 35 U.S.C. §112

Claims 1-36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite.

The Examiner asserts that the limitation "analysis environment" recited in claims 1, 12
and 28 is unclear because the specification does not define or fully and completely describe
"environment." The Examiner also asserts that the limitation "modeling environment" recited in
claims 5, 16 and 32 is unclear because the specification does not define or fully and completely
describe "environment." Applicants respectfully disagree.

Applicants submit that although the specification does not define "environment," those
of ordinary skill in the art in the field of Computer Science will appreciate that the term
"environment" may refer to "a particular configuration of hardware and software." For example,
the term "environment" may refer to a hardware platform and an operating system running on
the hardware platform.

Furthermore, The American Heritage® Dictionary of the English Language, Fourth
Edition, 2000 defines the term "environment" as follows in the field of Computer Science:

> a. The entire set of conditions under which one operates a
> computer, as it relates to the hardware, operating platform, or
> operating system.

   b. An area of a computer's memory used by the operating system
   and some programs to store certain variables to which they need
   frequent access.

In view of this, Applicants submit that although the term "environment" is not defined in the specification, those of ordinary skill in the art will appreciate the meaning of "environment" recited in claims 1, 5, 12, 16, 28 and 32.

The Examiner asserts that the limitation "biological process responsive to experimental results" recited in claims 1, 12, 22 and 28 is unclear. Applicants have amended claims 1, 12, 22 and 28 to further clarify the scope of the invention, thus rendering this rejection moot.

The Examiner also asserts that the limitation "experimental results generated by an in-situ experiment conducted on an experimental platform" recited in claims 1, 22 and 28 is unclear. Applicants have amended claims 1, 22 and 28 to further clarify the scope of the invention, thus rendering this rejection moot.

The Examiner further asserts that the limitation "experimental platform" recited in claims 1, 12, 22 and 28 is unclear. Applicants have amended claims 1, 12, 22 and 28 to clarify that the experimental platform is an experimental device.

The Examiner asserts that the limitation "said analysis environment gathering data ...and comparing the result" recited in claim 1 is unclear. Applicants have amended claim 1 to clarify the structural feature of the analysis environment.

The Examiner also maintains that the limitation "generates an event" recited in claims 4 and 15 is unclear. Applicants have amended claims 4 and 15 to clarify that the analysis environment generates an event signal when the difference between the expected result generated by the simulation engine and the data gathered from the device exceeds a predetermined threshold.

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The Examiner further asserts that it is unclear in what way claim 12 achieve the purpose of the preamble. Applicants have amended claim 12 to add the step of modifying the model of the biological process.

Furthermore, Applicants have amended claim 22 to change the limitation "chemical experiment" to "in situ experiment" to more closely follow the scope of the elected claims.

In view of the foregoing amendments and arguments, Applicants respectfully request that the Examiner withdraw the rejection of claims 1-36 under 35 U.S.C. §112, second paragraph.

VI.   Claim Rejections under 35 U.S.C. §102 (Goryanin *et al.*)

Claims 1-9, 11, 22, 23, 25-27, 28-30 and 32-36 are rejected under 35 U.S.C. 102(b) as being anticipated by Goryanin *et al.* (Bioinfomatics, 1999, Vol. 15, No. 9, p.749-758). Applicants respectfully traverse the rejection.

A.   Claims 1, 22 and 28

Applicants respectfully submit that Goryanin *et al.* fails to disclose at least one of the following features: "experimental results generated by an in situ experiment conducted on an experimental device" and "comparing the expected result to data gathered from said experimental device," as recited by claims 1, 22 and 28.

Goryanin *et al.* is generally directed to the creation and facilitation of analysis of mathematical models of cellular metabolism and physiology. Goryanin *et al.* discloses a mathematical simulation workbench, DBsolve, that helps create and analyze the mathematical models. DBsolve combines: (i) derivation of large-scale mathematical models from metabolic reconstructions and other data sources; (ii) solving and parameter continuation of non-linear algebraic equations (NAEs), including metabolic control analysis; (iii) solving the non-linear stiff systems of ordinary differential equations (ODEs); (iv) bifurcation analysis of ODEs; (v) parameter fitting to experimental data or functional criteria based on constrained optimization. (See Goryanin *et al.*, Abstract).

Applicants respectfully submit that Goryanin *et al.* does not disclose that the experimental data is gathered from an in situ experiment conducted on an experimental device. The "experimental data" of Goryanin *et al.* is the data that is observed and entered by a user, not experimental results generated by an in situ experiment on an experimental device. No mention of an experimental device is made in Goryanin *et al.,* and the system of Goryanin *et al.* is not disclosed to be adapted to be gathering results from the experimental device, as recited in claims 1, 22 and 28.

Additionally, Goryanin *et al.* fails to disclose the feature comparing the expected result to data gathered from the experimental device. The Examiner points to the following language (see office action, page 8) at page 753, column 2, paragraph 2 as disclosing this feature:

> This method can be used either to fit as model to experimental data (thereby discovering the values with appropriate error margins of the model's parameters under the conditions of the experiment), or to optimize a model to meet specified criteria (to discover how and which parameters should be changed to produce the specified optimum). For fitting, the method of generating the theoretical curves is specified on the Experimental Data page and the "Use Experimental Data" box is checked. Constraints can be imposed by pressing the Parameters button and defining the initial, boundary and step values for specified parameters. The fitting/optimization employs wither a zero-order (Hooke and Jeeves, 1961) or first-order (Levenberg, 1944; Marquardt, 1963) algorithm. Fitting procedures always face difficulties cased by multiple minima, which may be a particular problem when many parameters are involved. The 'best' fit might not be easily found; however, to check the quality of the procedure, the standard deviation and confidence intervals for every active parameter as well as an ANOVA table are shown in the Message window to help users make their assessment.

Applicants respectfully disagree with the Examiner's assertions. Goryanin *et al.* merely discloses a fitter for refining models using experimental data. Goryanin *et al.* does not teach or suggest comparing the expected result to data gathered from the experimental device, as recited by claims 1, 22 and 28.

In view of the above arguments and the amendments to claims 1, 22 and 28, Applicants respectfully request withdrawal of the rejection of claims 1, 22 and 28.

B.   Claims 2-9, 11, 23, 25-27, 29-30 and 32-36

Claims 2-9 and 11 depend on base claim 1 and, as such, incorporate all of the features of claim 1. Accordingly, claims 2-9 and 11 are novel for at least the reasons set forth above with respect to claim 1. Applicants respectfully request withdrawal of the rejection of claims 2-9 and 11.

Claims 23 and 25-27 depend on base claim 22 and, as such, incorporate all of the features of claim 22. Accordingly claims 23 and 25-27 are novel for at least the reasons set forth above with respect to claim 22. Applicants respectfully request withdrawal of the rejection of claims 23 and 25-27.

Claims 29-30 and 32-36 depend on base claim 28 and, as such, incorporate all of the features of claim 28. Accordingly claims 29-30 and 32-36 are novel for at least the reasons set forth above with respect to claim 28. Applicants respectfully request withdrawal of the rejection of claims 29-30 and 32-36.

VII.   Claim Rejections under 35 U.S.C. §102 (DelaFuente *et al.*)

Claim 1-2 and 10 are rejected under 35 U.S.C. 102(b) as being anticipated by DelaFuente *et al.* (Proceedings of the Second International Conference on System Biology, Pasadena, California, 2001, p213-221). Applicants respectfully traverse the rejection.

A.   Claim 1

Applicants respectfully submit that DelaFuente *et al.* fails to disclose each and every element of claim 1. Specifically, Applicants submit that DelaFuente *et al.* does not disclose at least the following feature: "an analysis environment in communication with said simulation engine, said analysis environment gathering data from said experimental device and comparing the expected result to data gathered from said device," as recited by claim 1.

DelaFuente *et al.* is generally directed to a method for reverse engineering gene regulatory networks from microarray gene expression data. DelaFuente *et al.* discloses the method as follows:

> 1. Select the set of n genes for which the regulatory network will be investigated (all genes of a genome of a subset thereof).
> 2. Perturb the ratio of transcription of one single gene.
> 3. Measure gene expression ratio between the new steady state reached after the perturbation and the reference state, using microarray or DNA chip technology.
> 4. Use fluorescence ratio FR and Eq. 6 to calculate n2 co-control coefficients, completing one row of each of the n co-control matrices.
> 5. Carry out steps 2-4 until all transcription rates in the initially selected set have been perturbed and gradually fill in the co-control matrices.
> 6. Invert the n co-control matrices to obtain n regulatory strength matrices Ri.
> 7. From the n matrices Ri, use row I of each to reconstruct the gene regulatory network.

(See DelaFuente *et al.*, page 215, right column).

DelaFuente *et al.* discloses the construction of a gene regulatory network from the measurement of gene expression ratios using microarray technologies. DelaFuente *et al.*, however, does not disclose gathering data from the experimental device and comparing the expected result to data gathered from the device.

The Examiner points to the following language (see office action, page 9) at page 216, column 2, paragraph 2 as disclosing this feature:

> Keeping in mind that small changes in transcription rates are difficult to achieve in practice and/or their effects are even harder to measure, we explored the performance of the method with larger perturbations (under-expression by 50% and over-expression by 200%). The values of the regulatory strengths obtained with these larger perturbations are compared to the theoretical values (calculated in Eq. 3 using elasticity and control coefficients obtained with the simulation software) in Table 1. Table 1 clearly shows that the error due to the finite differences

approximation in our method is relatively small for a small
perturbation (1.1x) but grows with larger perturbations (0.5x and
2x). Nevertheless, even with larger perturbations the absolute
error is less than 0.075 (17%), which we believe is well below the
measurement noise, and thus perfectly acceptable.

Applicants respectfully disagree with the Examiner's assertions. DelaFuente *et al.*
discloses a computer simulation of the reverse engineering method. The computer simulation
simulates the experiments to produce simulated data. (See DelaFuente *et al.*, page 215, right
column, section 3.1). There is no disclosure in DelaFuente *et al.* about the comparison of the
simulation result of a model with in-situ experimental data. Instead, the portion of DelaFuente
et al. pointed to by the Examiner, discloses that the values of the regulatory strength obtained by
the computer simulation are compared to the theoretical value calculated by Eq. 3. DelaFuente
et al. discloses in Table 1 the theoretical values calculated by Eq. 3 and the values obtained by
the computer-simulated experiments (1.1x perturbation, 0.5x perturbation, 2x perturbation).
That is, DelaFuente *et al.* discloses comparing simulation result of the model with the theoretical
values, not with the in-situ experimental data gathered from the experimental device, as recited
by claim 1.

In view of the above arguments and the amendments to claim 1, Applicants respectfully
request withdrawal of the rejection of claim 1.

B.   Claims 2 and 10

Claims 2 and 10 depend on base claim 1 and, as such, incorporate all of the features of
claim 1. Accordingly, claims 2 and 10 are novel for at least the reasons set forth above with
respect to claim 1. Applicants respectfully request withdrawal of the rejection of claims 2 and
10.

VIII.   Claim Rejections under 35 U.S.C. §102 (Potts *et al.*)

Claims 12-19 and 21 are rejected under 35 U.S.C. 102(e) as being anticipated by Potts *et
al.* (U.S. Patent No. 6,882,940).

A. Claim 12

Applicants respectfully submit that Potts *et al.* fails to disclose "comparing, by an analysis environment, the generated expected result to data gathered from said experimental device," where the expected result has been generated by a simulation engine based on the model of a biological process, as recited by claim 12.

The Examiner points to the following language at column 3, lines 40-60 as anticipating generating the expected result and comparing it to gathered experimental data (see, Office Action page 9):

> In one embodiment, the glucose monitoring system comprises, in operative combination, a sensing mechanism (in operative contact with the subject or with a glucose-containing sample extracted from the subject, wherein the sensing mechanism obtains a raw signal specifically related to glucose amount or concentration in the subject), a device to obtain either skin conductance readings or temperature readings from the subject, and one or more microprocessors in operative communication with the sensing mechanism. The microprocessors comprise programming to (i) control the sensing mechanism to obtain a series of raw signals at selected time intervals, (ii) correlate the raw signals with measurement values indicative of the amount or concentration of glucose present in the subject to obtain a series of measurement values, (iii) when necessary predict a measurement value at a further time interval, which occurs after the series of measurement values is obtained, (iv) compare the predicted measurement value to a predetermined threshold value or range of values, wherein a predicted measurement value lower than the predetermined threshold value is designated to be hypoglycemic,

Applicants respectfully disagree with the Examiner's assertions. As can be seen from the above quote, Potts *et al.* gathers measurement data, generates predictive values based on that data and a predictive model and then compares the predicted values with the threshold. That is, Potts *et al.* does not teach or suggest comparing the gathered data itself to the results of the simulation of the model. Instead, the gathered data is used as an *input* to the simulation. *Potts et al.* does not disclose comparing predicted expected result generated based on the model of the biological process with the experimental data, as recited by claim 12.

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In view of the above arguments and the amendments to claim 12, Applicants respectfully request withdrawal of the rejection of claim 12.

B.   Claims 13-19 and 21

Claims 13-19 and 21 depend on base claim 12 and, as such, incorporate all of the features of claim 12. Accordingly, claims 13-19 and 21 are novel for at least the reasons set forth above with respect to claim 12. Applicants respectfully request withdrawal of the rejection of claims 12-19 and 21.

IX.   Claim Rejections under 35 U.S.C. §103

Claims 12, 13, 14, 20 and 21 are rejected under 35 U.S.C. §103(a) as being unpatentable over DelaFuente *et al.* (Proceedings of the Second International Conference on System Biology, Pasadena, California, 2001, p213-221) in view of Bubendorf *et al.* (Journal of Pathology, 2001, Vol. 195, p.72-79). Applicants respectfully traverse the rejection.

A.   Claims 12

Applicants respectfully submit that DelaFuente *et al.* and Bubendorf *et al.* do not teach or suggest "comparing, by an analysis environment, the generated expected result to data gathered from said experimental device," as recited by claim 12.

The Examiner recognizes that DelaFuente *et al.* does not teach the use of an in situ experiment. Bubendorf *et al.* is cited to provide teachings for an in situ experiment. Bubendorf *et al.* teaches Tissue microarray (TMA) technologies. The Bubendorf *et al.* abstract states:

> Tissue microarray (TMA) technology allows a massive
> acceleration of studies correlating molecular in situ findings with
> clinico-pathological information. In this technique, cylindrical
> tissue samples are taken from up to 1000 different archival tissue
> blocks and subsequently placed into one empty 'recipient' paraffin
> block. Sections from TMA blocks can be used for all different
> types of in situ tissue analyses including immunohistochemistry
> and in situ hybridization.

Although Bubendorf *et al.* teaches in situ experiments, Bubendorf *et al.* does not teach simulating a model of a biological process to generate expected results and comparing the results with data gathered from the in situ experiment. Therefore, Bubendorf *et al.* and DelaFuente *et al.*, alone or in combination, do not teach or suggest gathering data relating to the experiment and comparing, by an analysis environment, the generated expected result to data gathered from said experiment, as recited in claim 12.

In view of the above arguments and the amendments to claim 12, Applicants respectfully request withdrawal of the rejection of claim 12.

B.   Claims 13, 14, 20 and 21

Claims 13, 14, 20 and 21 depend on base claim 12 and, as such, incorporate all of the features of claim 12. Accordingly, claims 13, 14, 20 and 21 are not rendered obvious over the cited references for at least the same reasons as above. Applicants respectfully request withdrawal of the rejection of claims 13, 14, 20 and 21.

X. Conclusion

In light of the aforementioned arguments, Applicants submit that the cited prior art references fail to disclose, teach or suggest the patentable features of the invention, and contends that the claimed invention is novel and non-obvious in view of the references.

Please charge any shortage or credit any overpayment of fees to our Deposit Account No. 12-0080, under Order No. MWS-109. In the event that a petition for an extension of time is required to be submitted herewith, and the requisite petition does not accompany this response, the undersigned hereby petitions under 37 C.F.R. §1.136(a) for an extension of time for as many months as are required to render this submission timely. Any fee due is authorized to be charged to the aforementioned Deposit Account.

In view of the above comments, Applicants believe that the pending application is in condition for allowance and urges the Examiner to pass the claims to allowance. Should the Examiner feel that a teleconference would expedite the prosecution of this application, the Examiner is urged to contact the Applicant's attorney at (617) 227-7400.

Dated: February 2, 2007   Respectfully submitted,

                                                By

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